

ethinylestradiol dose is 33% lower and also the total dose per cycle is 27% lower.

The advantages of a combination preparation for oral contraception to be administered over 23 days relative to the usual 21-day preparations with less than 30 μg of ethinylestradiol can be characterized as follows:

1. A significantly lower frequency of follicular developments in the user (maximum of 13% in females who received the 23-day preparation relative to a maximum of 40% among those who received the 21-day preparation). This means a greater contraceptive reliability of the 23-day preparation, especially in the case of previous intake errors. The danger of "breakthrough ovulations" is smaller.

2. The occurrence of large follicles of more than a 30 mm diameter is extremely rare. The development of ovarian cysts is improbable with the 23-day preparation in comparison to the 21-day preparation.

3. The recruitment of dominant follicles is suppressed in the shortened intake-free pause.

4. The endogenous 17β -estradiol levels are suppressed easily controllably in the case of the majority of the users of the 23-day preparation. Clinical symptoms such as breast tenderness, premenstrual syndrome and menstrual disorders, which can be attributed to increased and greatly fluctuating estrogen levels, are observed with the 23-day preparation with clearly lower frequency.

In summary, an intake, extended by two (or three) days, of preparations containing 20 μg of ethinylestradiol in each daily dosage unit can produce the above-mentioned advantages, without the daily dose having to be raised to the previously largely used level of 30 μg of ethinylestradiol.

The formulation of an estrogen and gestagen for the use according to the intention or for a combination preparation according to the invention takes place completely analogously as it is already known for usual oral contraceptives with 21-day intake period of the active ingredients, such as, for example, Femovan® (ethinylestradiol/gestodene) or Microgynon® (ethinylestradiol/levonorgestrel).

A pack containing a combination preparation according to the invention is also designed analogously to packs for already known oral contraceptives on the market with the variation that instead of the usual 21 dosage units containing the active components, now 23 or 24 such dosage units and 5 or 4 sugar pills are present or else contain other suitable indications that 5 or 4 days are to be bridged over until continuation of the intake of active ingredient-containing dosage units.

Moreover, reference is made to the statements made in EP-A 0 253 607, especially also to the statements there for determination of equivalent amounts of ethinylestradiol and 17β -estradiol, on the one hand, and various gestagens, such as levonorgestrel, desogestrel, 3-ketodesogestrel and gestodene, on the other hand.

For further details for the determination of dose equivalents of various gestagenic active ingredients, reference is made to "Probleme der Dosisfindung: Sexualhormone" [Problems of Dose-Finding: Sex Hormones]; F. Neumann et al. in "Arzneimittelforschung" (Pharmaceutical Agent Research) 27, 2a, 296-318 (1977), as well as to "Aktuelle Entwicklungen in der hormonalen Kontrazeption" [Current Developments in Hormonal Contraception]; H. Kuhl in Gynäkologie" [Gynecologist] 25: 231-240 (1992).

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1: Area with the 17β -estradiol level in groups of 30 females, who are treated with an oral contraceptive (75 μg of gestodene+20 μg of ethinylestradiol) in 21- or 23-day administration interval over three cycles.

FIG. 2: Number of females in %, who showed follicular developments (>13 mm diameter) with 21- or 23-day treatment with an oral contraceptive (75 μg of gestodene+20 μg of ethinylestradiol).

We claim:

1. A combination product for oral contraception, comprising

(a) 23 or 24 dosage units, each containing an estrogen selected from
>2.0 to 6.0 mg of 17β -estradiol and
0.020 mg of ethinylestradiol;

and a gestagen selected from
[0.25 to 0.30] 2.5 to 3.0 mg of drospirenone and
[0.1 to 0.2] 1 to 2 mg of cyproterone acetate,

and
b) 5 or 4, respectively, active ingredient-free placebo pills or other indications to show that the daily administration of the 23 or 24 dosage units respectively, is to be followed by 5 or 4, respectively pill-free or placebo pill days.

2. A combination preparation for oral contraception according to claim 1, wherein the estrogen is ethinylestradiol.

3. A combination preparation of claim 2, wherein the gestagen is cyproterone acetate.

4. A combination preparation of claim 2, wherein the gestagen is drospirenone.

[5. A combination preparation according to claim 1, wherein the estrogen is present in a dose of 20 μg of ethinylestradiol or an equivalent dose of 17β -estradiol and the gestagen is present in a dose equivalent to 75 μg of gestadene.]

6. A combination preparation according to claim 1, which comprises 23 dosage units and 5 placebo pills or other indications to show that no dosage unit or a placebo pill is administered during the last 5 days of the menstrual cycle.

[7. A combination preparation according to claim 1, which comprises 23 dosage units, each containing 20 μg of ethinylestradiol and a dose of cyproterone acetate or drospirenone equivalent to 75 μg of gestodene and 5 placebo pills or other indications to show that no dosage unit or a placebo pill is administered during the last 5 days of the menstrual cycle.]

8. A combination preparation of claim 1, wherein the estrogen is 17β -estradiol.

9. A combination preparation of claim 8, wherein the gestagen is cyproterone acetate.

10. A combination preparation of claim 8, wherein the gestagen is drospirenone.

11. A combination preparation of claim 4, which comprises 23 dosage units and 5 placebo pills or other indications to show that no dosage unit or placebo pill is administered during the last 5 days of the menstrual cycle.

12. A combination preparation of claim 4, which comprises 24 dosage units and 4 placebo pills or other indications to show that no dosage unit or placebo pill is administered during the last 4 days of the menstrual cycle.

13. A combination product for oral contraception, comprising

(a) 23 or 24 daily dosage units, each containing
0.020 mg of ethinylestradiol, and
2.5 to 3.0 mg of drospirenone,
and

(b) 5 or 4, respectively, active ingredient-free placebo pills or other indications to show that the daily administration of the 23 or 24 dosage units, respectively, is to be followed by 5 or 4, respectively, pill-free or placebo pill days,